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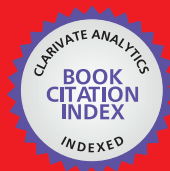
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Cyclodextrin-Based Nanofibers and Membranes: Fabrication, Properties and Applications

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Abstract

Cyclodextrin (CD)-based electrospun nanofibers have become critical role players in the water treatment arena due to their high porosities, small diameters, high surface area-to-volume ratio and other unique properties they exhibit. Investigations demonstrate that nanofibers containing CD molecules can be facially blended with other polymeric species and/or photocatalytic and magnetic nanoparticles to enhance their rates of adsorption, inclusion complexation and selective photodegradation. These properties make them excellent candidates for the removal of water pollutants. On the other hand, the electrospinning process has become the method of choice in the fabrication of various types of CD nanofibrous mats due to its versatility, cost-effectiveness and its potential for the mass production of uniform nanofibers. CDs and CD-derivatives have also found application in membrane technologies, particularly in mixed matrix and thin film composite membranes. CD-blended membranes display improved performances in terms of selectivity, rejection, permeation and flux with reduced fouling propensities and can be used for drinking water purification and removal of emerging micropollutants. This chapter critically reviews CD-based electrospun nanofibers looking at their production, characterization methods and various applications. The use of CDs as membrane materials and how they can be fully explored in water treatment are also investigated.

Keywords: cyclodextrins, electrospun nanofibers, membranes, adsorption, inclusion complexation, water treatment

1. Introduction

Common water pollutants such as toxic micro-organisms and inorganic and organic waste are a serious threat to the health of humans, animals and the aquatic biota. Diverse methods and materials are currently used to treat wastewater in order to overcome the high level of water pollution. However, emerging micropollutants (EMPs) such as hormones, pharmaceuticals, detergents, phenols, fragrances, illicit drugs, endocrine disruptors, steroids and personal care products have proven to be persistent and difficult to remove from aqueous systems [1, 2]. In particular, EMPs are continuously found in trace amounts in waste and treated water. In addition, trace organic pollutants find their way into wastewater after being excreted from human bodies and when disposed to the sewage system [1–3]. Pharmaceutical waste and other trace organic pollutants leave the wastewater treatment plant without being treated because they are present in small amounts, biologically active or thermally and chemically stable [2]. EMPs and their derivatives are of great concern since their fate and behavior is not well understood. Moreover, current treatment methods are not effective in the removal of these EMPs. This has therefore led to the development of diverse technologies including nanotechnology-based technologies to remove EMPs in water systems.

Nanotechnology-based techniques frequently applied in water treatment make use of various nanomaterials including, among others, nanofibers, nanowires, nanotubes, nanorods and nanospheres. These distinct nanomaterials are endowed with several advantageous properties that render them suitable in the removal of micropollutants from aqueous systems. These properties include high porosity, small diameters and high surface area per unit volume. In particular, nanofibers are easy to handle, reusable and recyclable making them ideal candidates for use in water treatment applications [4, 5]. Workers have also applied photocatalytic nanomaterials such as TiO_2 and ZnO and found them to be excellent candidates for use in the photodegradation of most micropollutants using their inherent quantum and surface properties [6]. TiO_2 and ZnO nanomaterials have been applied in various areas, which include textile, wastewater treatment, particulate separation, health care, desalination, energy, liquid filtration and sensors [7, 8]. Hollow-structured nanomaterials such as nanotubes and nanofibers (**Figure 1**) can encapsulate active additives such as photocatalysts, antioxidants and antibacterial agents and then applied in water treatment, food packaging and biotechnology [8, 9]. Photocatalysts have been incorporated with other materials such as the natural polymer cyclodextrins (CDs) for use in water treatment applications [10]. CDs are gaining extensive popularity as adsorbents and as membrane materials due to their toroidal structure and distinct characteristics.

CDs and their derivatives such as methyl- β CD (m- β CD) (**Figure 2**) are known to significantly remove organic pollutants from water systems *via* adsorption and inclusion complexation. They can also be polymerized to form supramolecular structures with high surface areas [12]. The geometry of CDs demonstrates a hydrophobic cavity capable of inclusion complexation with a wide range of pollutants [7, 13]. The ability of CDs to capture and form inclusion complexes with other molecules in solution and their ability to be electrospun with ease as well as other physicochemical properties render them ideal candidates for water treatment applications [7, 12, 14]. The release of water molecules from the hydrophobic cavity, coupled with

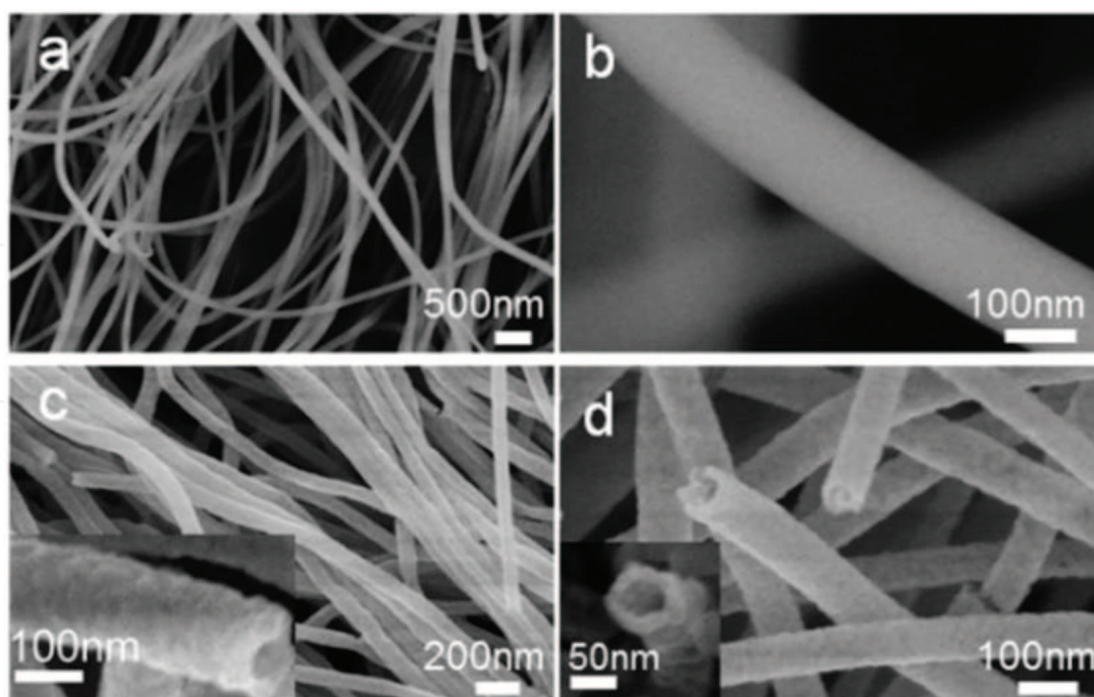


Figure 1. Microscopic view of hollow-structured nanofibers (a and b) the as-electrospun nanofibers. (c and d) The images of nanotubes at low and high magnification. The inset shows the surface and cross profile of the nanotube. Reproduced with permission from [11].

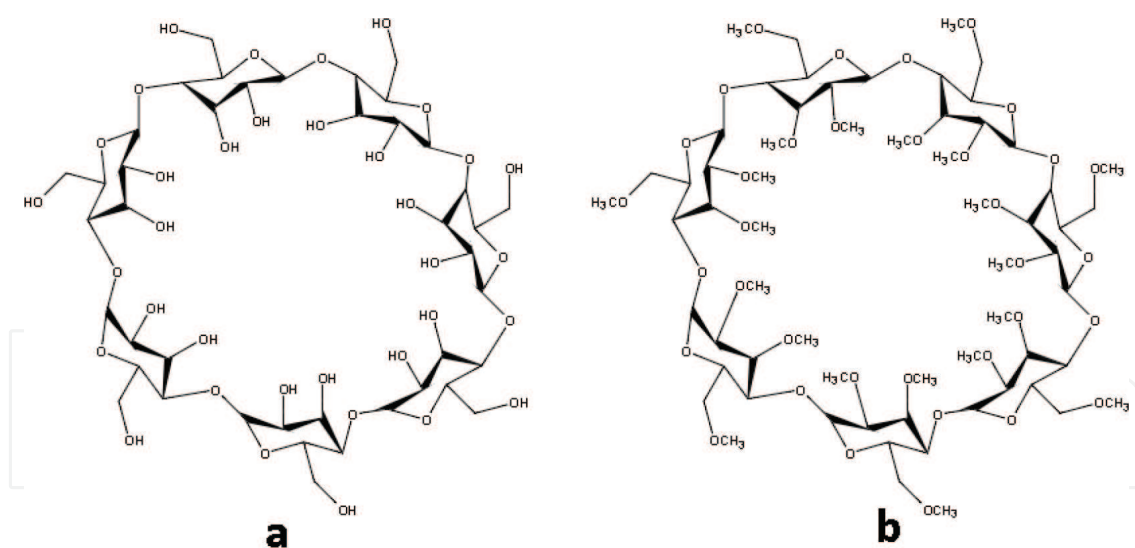


Figure 2. Schematic illustration of (a) β CD and (b) m- β CD.

hydrogen bonding, charge transfer interactions, hydrophobic interactions, van der Waals interactions, release of conformational strain and electrostatic interactions are the driving forces for inclusion complexation through apolar-apolar interaction of CDs and the guest compounds [12, 15]. It is for this reason that CDs are used in water treatment to remove EMPs and various other pollutants as well as in medicine for drug delivery applications. Besides

their use in nanofiber production, CDs and their derivatives have become popular in membrane technology.

Recently, workers prepared electrospun nanofibers using chitosan and incorporated silver and iron nanoparticles for water disinfection processes. These nanofibers were later effectively modified using CDs and cellulose to increase their thermal and chemical stability [16]. Somewhere else, thermally and mechanically stable β CD/cellulose acetate nanofibers were synthesized using an environmentally benign procedure and used for enhanced antimicrobial treatment of water [17]. In membrane technology, Adams et al. utilized CD molecules as modifying agents for the preparation of polysulfone-polyurethane (PSF-PU) composite nanofiltration membranes, which were used for the removal of undesirable salts [18].

In this chapter, electrospun CD-based materials are discussed in view of water treatment, their properties and advantages toward improving current water treatment methods by removing EMPs in waste and treated water. We also critically investigate CD-based membrane techniques in terms of their production and characterization methods with focus placed on their application in water treatment. Other applications of these CD-based nanocomposites such as drug delivery, antimicrobial uses, biomedical uses, filtration, photocatalysis and environmental protection are covered.

2. Fabrication methods of nanofibers

Various methods are used in the production of nanofibers today. These include, among others, polymer blending, sea/island cross-section conjugation and electrospinning techniques [19, 20]. These technologies have several disadvantages that include sizes in the microscale instead of nanoscale and low tensile strength. They also form nonwoven sheets that need further treatment using organic solvents [21]. However, several researchers have described electrospinning as the best nanofiber fabrication method compared to the other methods. In the next sections, we explore the various methods of nanofiber production.

2.1. Polymer blend method

The polymer blend method is a method that uses two or more polymers to produce materials with superior properties [22]. This method is divided into three main categories, which are: miscible, immiscible and compatible polymer blending. To produce fibers with nanoscale diameters and uniform continuous length in large scale, this method is often coupled with the electrospinning method. In this way, blended polymer solutions can be electrospun to produce fibers with desired properties [23, 24].

Miscible polymer blends are characterized by a homogeneous morphology/mixture on the segment level; however, the local chain dynamic may exhibit different dependences on temperature and blend composition [25]. The presence of nanoheterogeneities has been observed in miscible polymer blends where Lodge and McLeish have described this as “self-concentration” [26]. This illustrates that high glass transition temperature components often have segmental dynamics much closer to the bulk blend, while the low glass transition temperature is closer to the pure component [25]. However, miscible polymers often have one glass transition

temperature that is dependent on the composition. Polymers can be miscible in melt state and immiscible in solid state due to fast crystallization of one component compared to the other [22]. When blended polymers do not crystallize at the same rate, it results in phase separation, which will affect the final product and their envisaged properties [22]. However, due to the miscibility of the components, they can each reside in the interlamellar and/or interspherulitic regions of each other during crystallization, thus reducing separation rates [27].

Immiscible solutions are often referred to as emulsions where one component is dispersed on top of the other as small-sized droplets depending on the quantity of each solution as shown in **Figure 3** [28]. Most polymer blends are immiscible because of the weak interfacial interactions between components and different molecular weight of each component [22]. Immiscible polymer blends also have enhanced properties compared to their separate components [29]. Immiscible polymer blends limit full access of each component properties and application due to their incompatibility. Producing nanofibers through this method requires the use of stabilizing agents such as fillers and metal organic frameworks. Produced fibers are in microscale and requires subsequent polymer matrix extraction [30, 31].

Compatible polymer blends are immiscible polymer blends that have uniform macroscopically physical properties. Compatible polymer blends are often used to enhance the properties of components such as elastic modulus, crystallinity and glass transition temperature [32, 33]. Polymers often require the use of fillers/compatibilizer to induce compatibility between the components (**Figure 4**). To be effective enough, fillers must have a particle radius of the same order of magnitude as the gyration radius of the polymers used. Examples of fillers include ethylene-acrylic acid and ethylene-vinyl alcohol [33, 34].

2.2. Sea/island cross-section conjugation

Sea or island cross-section conjugation is a type of a conjugate spinning method used to fabricate fibers with diameters of less than 1 μm with a predetermined component arrangement in its cross-section. Two polymer components of a conjugate type are elongated and extruded together from a spinneret. These polymers then combine in the back of a spinning nozzle. The produced conjugate fibers with two components are then split into filaments. This technique involves spinning a bicomponent filament consisting of polyester, polyethylene, nylon or polypropylene used as an island component and a polymer like polystyrene is used as a sea component. The fabric is then exposed to a solvent, thermal or mechanical treatment whereby the immiscible components separate as the polystyrene sea component dissolves in a solvent,

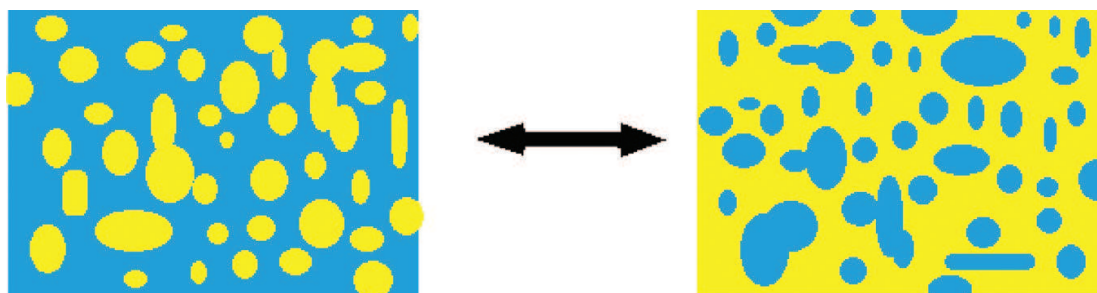


Figure 3. Schematic representation of immiscible polymer solution with varied concentrations of each polymer.



Figure 4. Illustration of the effects of compatibilizer or filler on compatible polymer blends.

which is a nonsolvent for the polyester island component after conventional processing into fibers. This results in individual polyester island filaments. The ratio of the two components in the ultrafine filament yarn, the shape and the number of the resulting individual segments can be varied depending on the design of the spinneret [20, 21].

2.3. Electrospinning technique

The electrospinning technique is a versatile, flexible and cost-effective method for producing nanofibers. It has become very attractive and common in the synthesis of nanofibers for various applications. Electrospinning is often preferred over other methods since it readily produces nanofibers from a number of materials, which include polymers, ceramics, composites and semiconductors [35, 36]. Electrospun nanofibers can be easily modified to improve certain properties. This can be achieved during electrospinning or by posttreatment methods [36–38].

Electrospinning can produce nanofibers of long length, diversified composition, high surface area-to-volume ratio, uniform diameter, flexible surface functionalities and superior mechanical properties [39]. In electrospinning, nanofibers are formed as the polymer solution is stretched between two surface charges and as the solvent evaporates due to electrostatic repulsion forces [40]. During electrospinning, a polymer solution in a syringe is stretched to the collector in a cone shape (Taylor cone) under high voltage. The collector screen used can be either a stationary flat screen or a rotating drum collector. The type of collector can greatly influence the morphology of the nanofibers [41]. The diameter, morphology and distribution of electrospun nanofibers depend on the applied voltage, solution viscosity, tip to collector distance, temperature and flow rate. **Figure 5** shows a setup of an electrospinning instrument with a flat stationary collector. The setup consists of a high-voltage supply, polymer solution in a syringe and the collector screen [42].

When the electrospinning parameters and polymer solution properties are not properly optimized, beaded fibers such as those depicted in **Figure 6(a)** can be obtained. On the other hand, when all the properties and parameters are precisely optimized, bead-free nanofibers such as those displayed in **Figure 6(b)** can be obtained [43]. In electrospinning, it is important to optimize all parameters including the polymer solution properties such as the concentration before spinning large quantities.

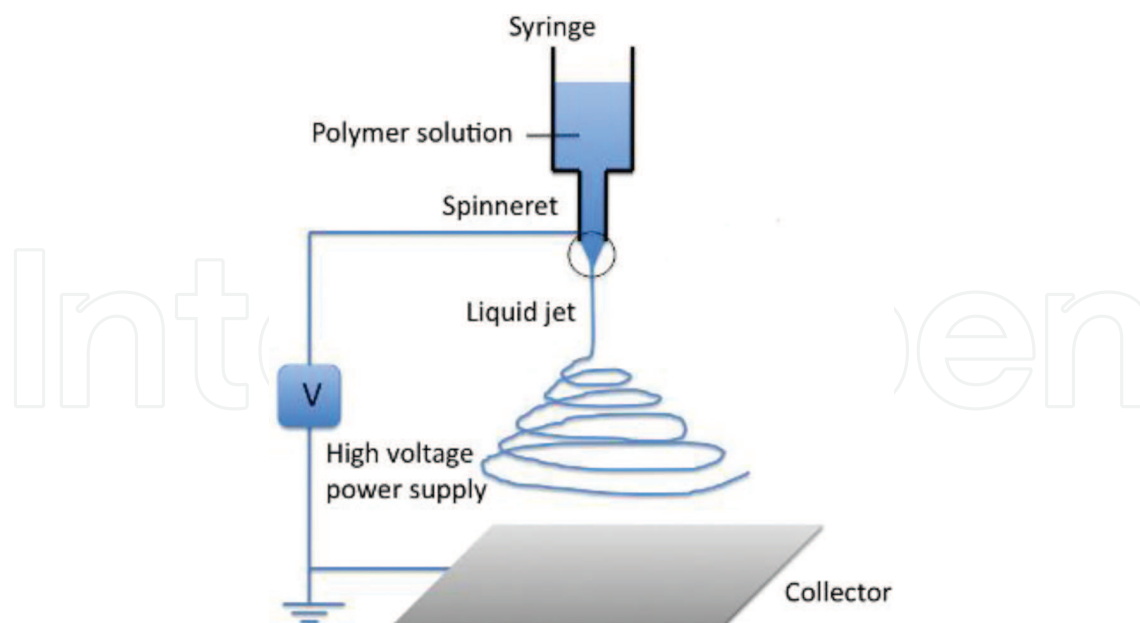


Figure 5. Schematic illustration of electrospinning setup with flat stationery collector. Reproduced with permission from [42].

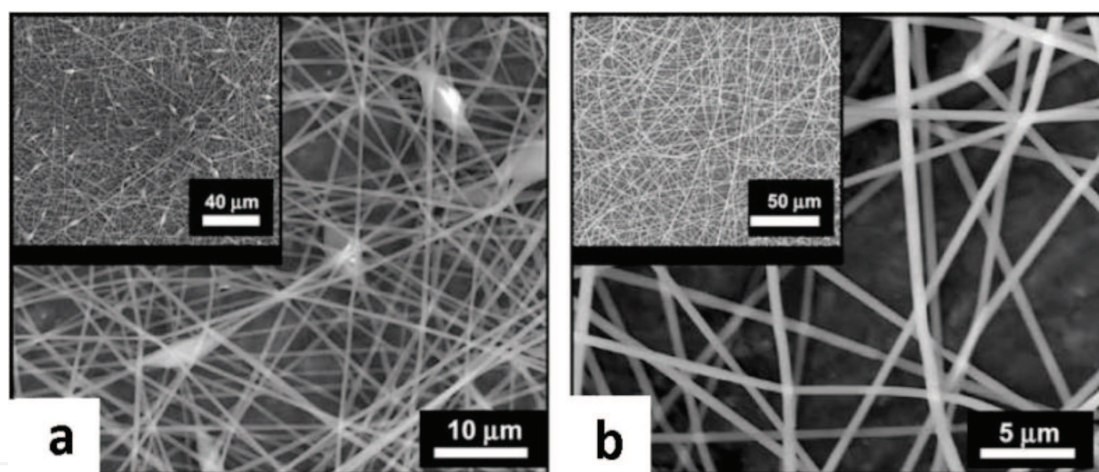


Figure 6. Microscopic representation of electrospun nanofibers without proper optimization (a) and with proper optimization (b) of all parameters. Reproduced with permission from [43].

2.3.1. Mechanism for the formation of electrospun CD nanofibers and influencing factors

Electrospinning CDs into nanofibers is still a challenging task because of their small cyclic structure. However, electrospinning these glucose derivatives would result in nanofibrous mats with excellent properties such as high surface area-to-volume ratio and high possibilities of specific surface functionalization [44, 45]. A number of factors can affect the electrospinning mechanism of CDs. Besides the fact that these cyclic oligosaccharides cannot be easily stretched into nanofibers, factors such as solvent type, concentration, copolymers and compatibility play a critical role in the successful electrospinning of CD nanofibers. Fortunately, CDs are soluble in most organic solvents such as water, dimethylacetamide, dimethyl sulfoxide

and dimethylformamide, with water and DMF being the most used solvents [46, 47]. **Figure 7** demonstrates that indeed the type of solvent used to prepare the solution has a pivotal effect on the formation and surface roughness of nanofibers. The most important factors to look at when choosing a solvent include the conductivity, density, solubility with other solvents and viscosity.

When electrospinning CDs, concentration also plays a critical role. At high concentrations, cyclic molecules like CDs and phospholipids can form aggregates and have sufficient electrostatic and intermolecular interactions [44, 48, 49]. The aggregation and molecular interaction act as chain entanglements making the molecules overlap and entangle like polymers in dilute solutions. **Figure 8** clearly depicts the low- and high-concentration effects on electrospun phospholipids and CDs. When using copolymers with CDs, the compatibility and dissolution of the two should be checked since this will affect the intramolecular interactions of the two polymers as well as the formation and morphology of the ultimate nanofibers [36, 47, 50, 51].

2.3.2. Polymer-free cyclodextrin nanofibers

As highlighted earlier, electrospinning cyclic polymers such as CDs is very challenging. However, CDs can form aggregates in their concentrated solution via intermolecular hydrogen bonding and interactions resulting in chain entanglements making it possible to electrospin CDs [44, 52].

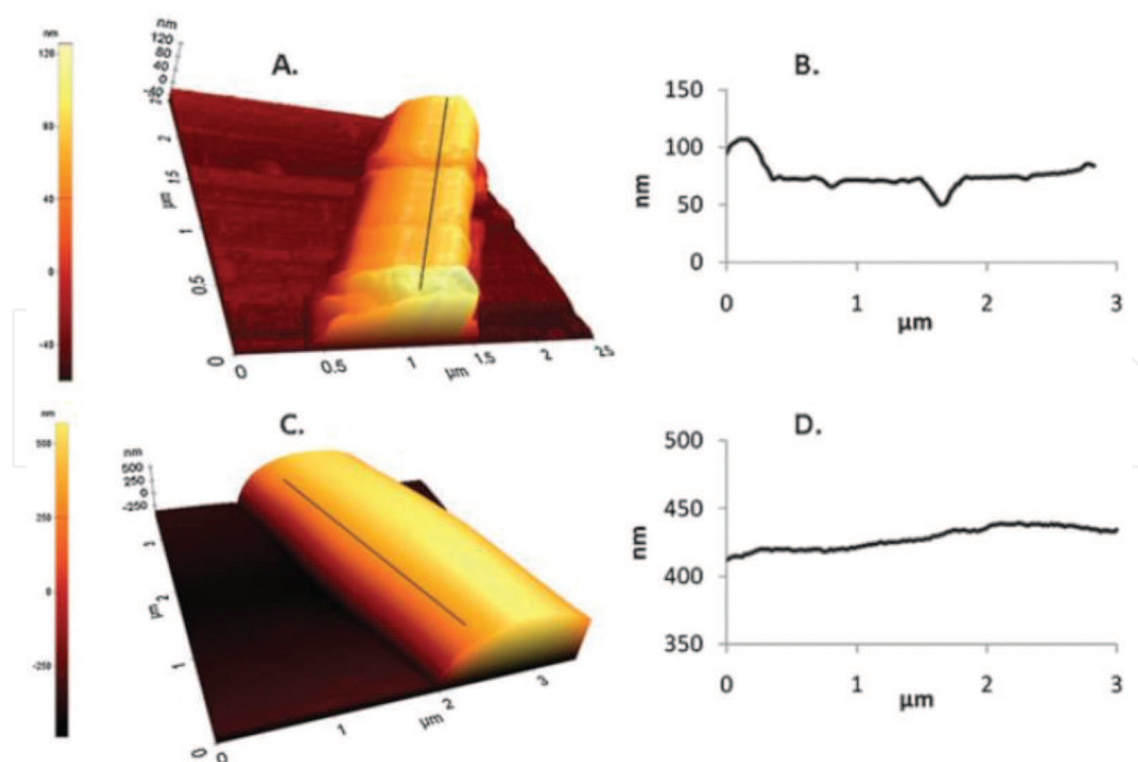


Figure 7. (A) AFM image and (B) fiber axis cross-section profile of the MβCD nanofiber prepared in water. (C) AFM image and (D) fiber axis cross-section profile of the MβCD nanofiber dissolved DMF. Reproduced with permission from [44].

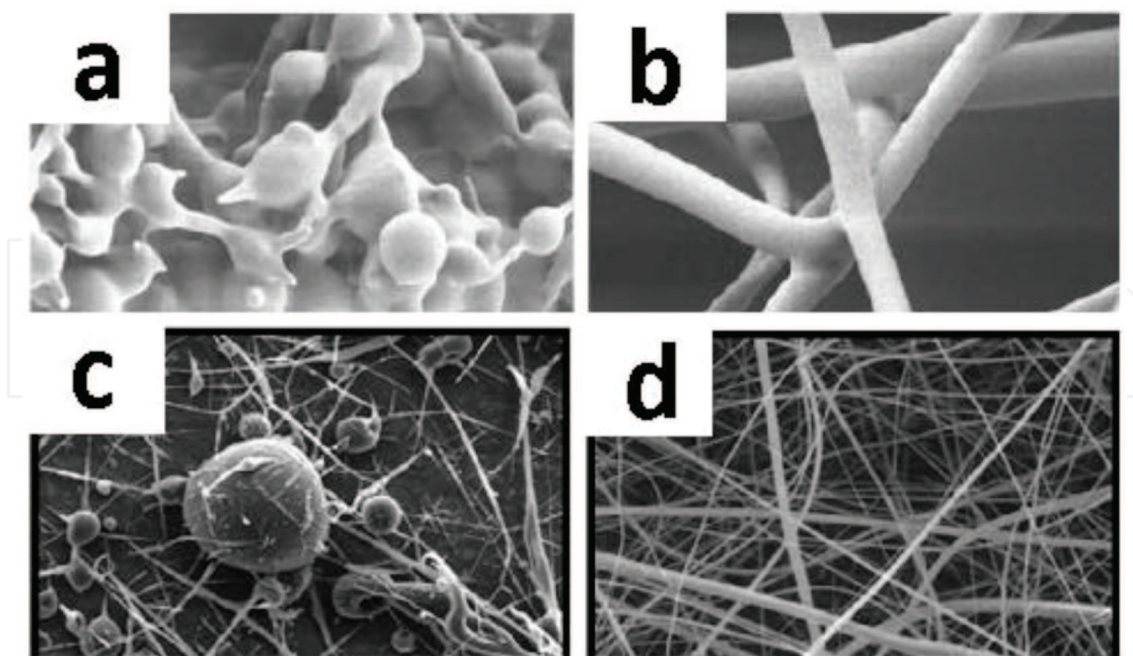


Figure 8. SEM micrographs revealing the concentration effect on electrospun phospholipids (a 35% and b 50%) and CD nanofibers (c and d) at low and high concentrations. Reproduced with permission from [49].

Celebioglu and Uyar reported the first successful electrospinning of carrier polymer-free CD nanofibers. In their report, highly concentrated solutions of methyl- β CD (140 and 160% w/v) were prepared in water and DMF. Electrospinning these solutions yielded nanofibers with diameter ranges of 20–100 and 100–1200 nm using water and DMF, respectively [44, 53]. At concentrations lower than 140% w/v, beaded nanofibers were obtained. They also reported another successful electrospinning of hydroxypropyl- β CD (HP- β CD) and HP- β CD inclusion complex with triclosan. Bead-free HP- β CD and HP- β CD/triclosan were obtained at higher concentrations of 160% w/v. **Figure 9** shows the SEM images of polymer-free HP- β CD and HP- γ CD nanofibers dissolved in DMF and water [52]. Celebioglu used HP- β CD and HP- γ CD for the entrapment of volatile organic compounds (VOCs), aniline and benzene [45]. The results indicated that CD nanofibers had better performances compared to powdered CDs, while β CD nanofibers performed better than γ CD nanofibers. The performance was dependent on the type of CDs, solvent and VOC type. Therefore, electrospinning of CDs and CD derivative nanofibers strongly depends on the type of CDs, solution concentration, solvent used and intermolecular interactions [46]. In **Table 1**, we show electrospun CD nanofibers prepared using different types of CD derivatives in different solvents without an additional polymer being used and the effect on the fiber sizes thereof.

2.3.3. Copolymerized cyclodextrin nanofibers

In order to improve the propensity of electrospinning CDs into excellent nanofibrous mats and take advantage of the CD properties, CDs can be blended with other polymers such as polyethylene terephthalate (PET), polyvinyl alcohol (PVA), polycaprolactone (PCL), poly(methyl methacrylate) (PMMA), polyvinylpyrrolidone (PVP), polylactic acid (PLA) and cellulose. This

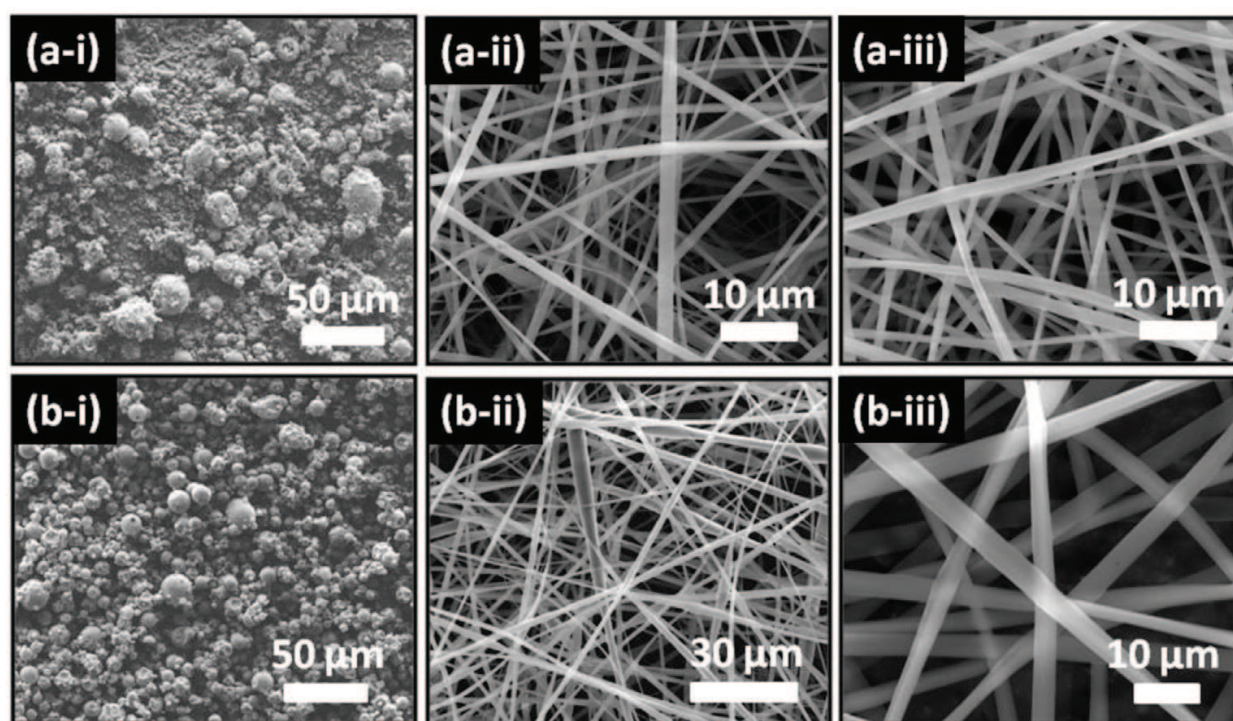


Figure 9. SEM images of (a-i) HP- β CD/powder, (a-ii) HP- β CD/water-nanofiber, (a-iii) HP- β CD/DMF-nanofiber, (b-i) HP- γ CD/powder, (b-ii) HP- γ CD/water-nanofiber and (b-iii) HP- γ CD/DMF-nanofiber. Reproduced with permission from [45].

CD-type	Solvent	Conc. (% w/v)	Method	Size (nm)	Ref
α and β CDs	Water, DMF, DMAc and DMSO	120–160	Electrospinning	80–940	[53]
HP- β CDs	Water	50–70	Electrospinning	933–990	[54]
M- β CDs, HP- β CDs and HP- γ CDs	Water, DMF and DMAc	100–160	Electrospinning	250–1860	[55]
HP- β CDs	Water	100–160	Electrospinning	200–1600	[52]
M- β CDs	Water and DMF	100–160	Electrospinning	20–1200	[44]

Table 1. Electrospun polymer-free CD nanofibers, conditions of preparation and size of nanofibers.

greatly improves the general properties of the nanofibers and expands their possible areas of application [19, 20, 50, 51, 56]. For example, **Figure 10** depicts electrospun CD-modified PS nanofibrous mats. Nanofibrous mats or membranes with high permeability are excellent candidates as microporous support substrates for thin film composite membranes with high flux and for application in microfiltration processes [57–60]. Copolymerization of cross-linked or modified CDs with other polymers reduces their solubility in water and makes them excellent candidates for water treatment applications.

Uyar and coworkers electrospun poly(methyl methacrylate) functionalized with CDs (PMMA/ β CDs) for the treatment of organic vapors. It was found that PMMA/ β CD nanofibers

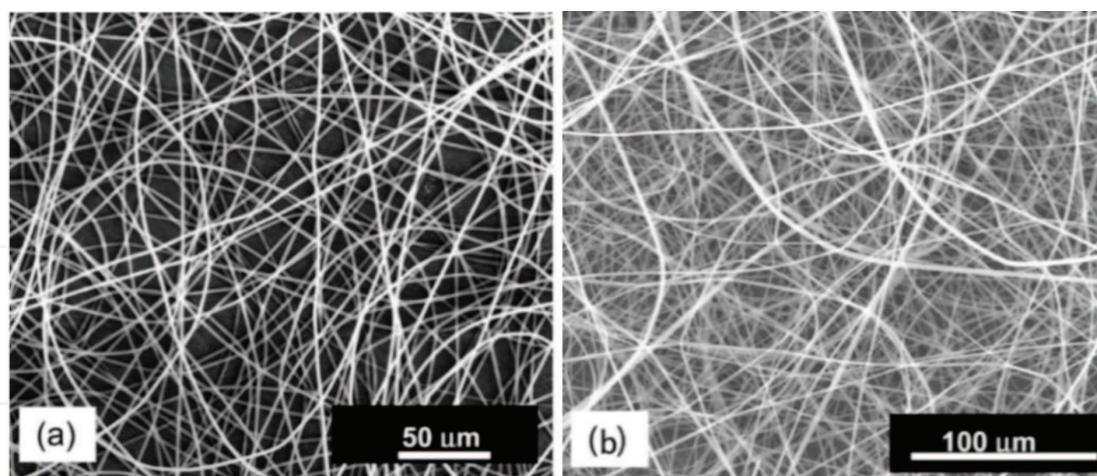


Figure 10. SEM micrographs for electrospun (a) PS and (b) PS- β CD nanofibers. Reproduced with permission from [46].

successfully encapsulated organic vapors such as aniline and styrene. The organics were inclusion complexed by β CD cones in solution [46]. CD/polymer nanofibers have also been used as reducing and stabilizing agents for other nanoparticles. Celebioglu et al. demonstrated this when they used polyvinyl alcohol/HP- β CD (PVA/HP- β CD) nanofibers as reducing and stabilizing agents for Ag nanoparticles. In this case, PVA was used as a primary agent, while HP- β CDs were used as secondary agents [56].

In water treatment, materials with high adsorption capacity are useful when it comes to the removal of pollutants such as dyes. Teng et al. used mesoporous PVA/SiO₂/ β CD nanofibers as adsorbents for the removal of indigo carmine dye in wastewater. The nanofibers were found to have adsorption capacities of up to 495 mg/g and equilibrium was reached in less than 40 min, due to the presence of CDs [61]. Zhang et al. prepared composite nanofibrous membranes from PVA/ β CDs using electrospinning for molecular entrapment of organics. It was found that these nanofibrous membranes could effectively and readily capture organic molecules. This was attributed to the inclusion complexation of organic molecules by the CDs. It was further suggested that these kinds of membranes can also be applied in areas such as drug delivery, separation/purification and electrochemical sensors, among others [62].

Research shows that copolymerized CD nanofibers and their derivatives find application in various areas due to the properties and advantages induced by the incorporation of CDs. **Table 2** shows various copolymerized CD nanofibrous mats and their applications.

2.3.4. CD nanofibers incorporated with nanoparticles

Blending electrospun CD nanofibers with nanomaterials results in unique properties from large surface area of nanofibers and excellent properties of the nanomaterials to specific structural and functional properties [67]. Nanomaterials supported on other materials have the disadvantage of low efficiency because of small interface surface available compared to powder photocatalysts. However, powdered nanomaterials cause secondary contamination with low recovery and require further treatment after usage. The high efficiency of powdered

CD type	Copolymer	Solvent	Method	Size (nm)	Application	Ref.
HP-βCDs	PVA	Deionized water	Electrospinning	290–485	Reducing and stabilizing agent for Ag antibacterial nanoparticles	[56]
βCDs	PCL	DMF and DCM	Electrospinning	336–389	Drug delivery of naproxen	[50]
βCDs	PMMA	DMF and toluene	Electrospinning	625–977	Organic vapor waste treatment	[51]
βCDs	PVC	DMF and THF	Electrospinning	420–450	Membrane modification	[19]
βCDs	Carbonaceous nanofiber membrane	Water	Electrospinning	120–144	Membrane filtration of phenolphthalein	[63]
βCDs	Cellulose	DMF	Electrospinning	100–800	Antibacterial activity (<i>E. coli</i> and <i>S. aureus</i>)	[20]
βCDs	PVP	Water and ethanol	Electrospinning	450	Stabilizing and reducing agent for Au nanoparticles	[47]
βCDs	Chitosan and PVA	Water and chloroacetic acid	Electrospinning	84–285	Drug delivery	[64]
α, β and γCDs	PET	TFA and DMF	Electrospinning	12.4–15.3	Phenanthrene removal in aqueous solutions	[7]
α, β and γCD-menthol IC	PS	DMF	Electrospinning	300–4250	Enhancement of durability and stability of fragrances	[65]
α, β and γCDs	PLA	DMF, DMSO and chloroform	Coprecipitation and electrospinning	140–1580	Antibacterial growth (<i>E. coli</i> and <i>S. aureus</i>)	[66]
α, β and γCDs	Zein	DMF	Electrospinning	90–185	—	[5]
α, β and γCDs	PMMA	DMF	Electrospinning	625–1024	Molecular filters and water treatment	[9]

Table 2. Electrospun copolymerized CD nanofibers, solvent type, sizes and their applications.

nanomaterials is outweighed by the recovery, recyclability and reusability of supported nanomaterials [68]. **Figure 11** shows SEM and TEM images of electrospun HP-βCD containing Au nanoparticles which also shows the d-spacing of 0.235 nm between Au {111} planes (**Figure 11**) [69].

CD nanofibers incorporated with nanoparticles have been prepared via electrospinning and self-assembly. These two techniques produced hierarchical structures of nano- to macroscale catalysts such as CD-TiO₂ and CD-ZnO [70, 71]. CD-TiO₂ nanofibers prepared by Yoon and Nichols displayed a hierarchical structure of nanoparticles interconnected into a 3D network as demonstrated in **Figure 12**. The 3D structure was found to have high surface area and large porosity [72, 73]. CD-TiO₂ composites have been found to be stable over a wide range of pH. Somewhere else, it was found that CDs guide the assembly of TiO₂ nanomaterials into nanowires hosted in a CD nanotube structure. In this process, CD molecules coat TiO₂ nanomaterials and produce long

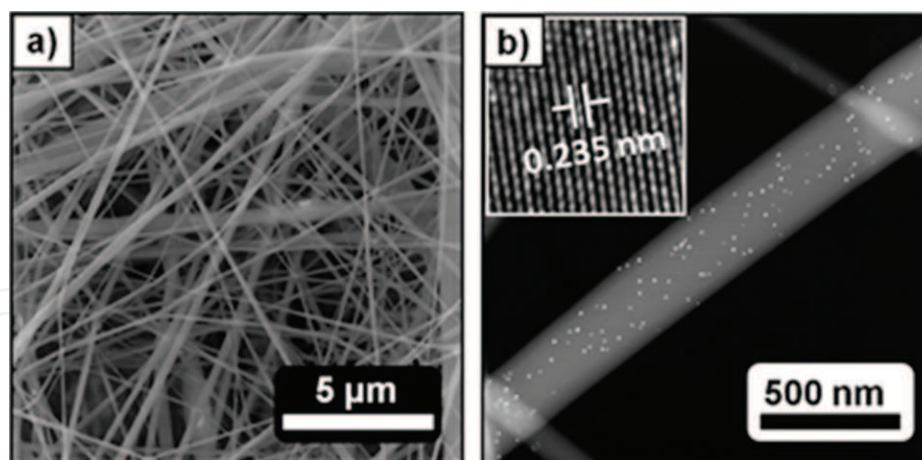


Figure 11. (a) SEM and (b) TEM images of electrospun HP- β CD nanofibers incorporated with Au nanoparticles. Inset HR-TEM image of a single Au-nanoparticle indicating the d-spacing between the planes [69].

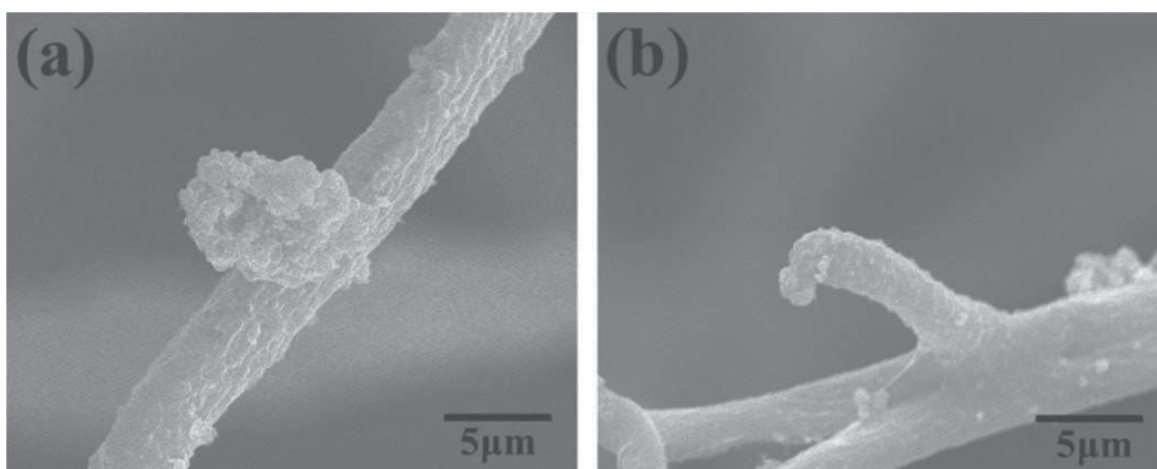


Figure 12. SEM images illustrating the 3D nature of CD-directed TiO_2 nanoparticles forming nanofibers (a) A small aggregate attached on the side of the nanofiber. (b) The aggregate smoothes and continues to grow into a new fiber. Reproduced with permission from [73].

CD- TiO_2 nanotubes. These CD- TiO_2 nanofiber catalysts have shown enhanced photodegradation of organic materials [74–76].

Using CDs, Zhao and Chen have also demonstrated the preparation of ZnO nanofibers and multipetals (**Figure 13**). When analyzed, the ZnO nanomaterials were decorated with CD molecules [77]. In another study, CD-ZnO nanofibers were synthesized under mild conditions of thermal decomposition [78, 79]. In their study, zinc acetate was coated with CD molecules and ZnO synthesis took place within the CD molecules resulting in CD-ZnO nanofibers. Rakshit and Vasudevan prepared CD-ZnO fibers with high degradation performance of Nile red [80]. In all these studies, CD-ZnO nanofibers were prepared using self-assembly processes.

CDs can also act as electron donors and molecular recognition agents when incorporated with photocatalytic nanoparticles [76]. CD chemisorption onto photocatalytic nanomaterials improve their stability against aggregation and enhance their charge transfer reactions.

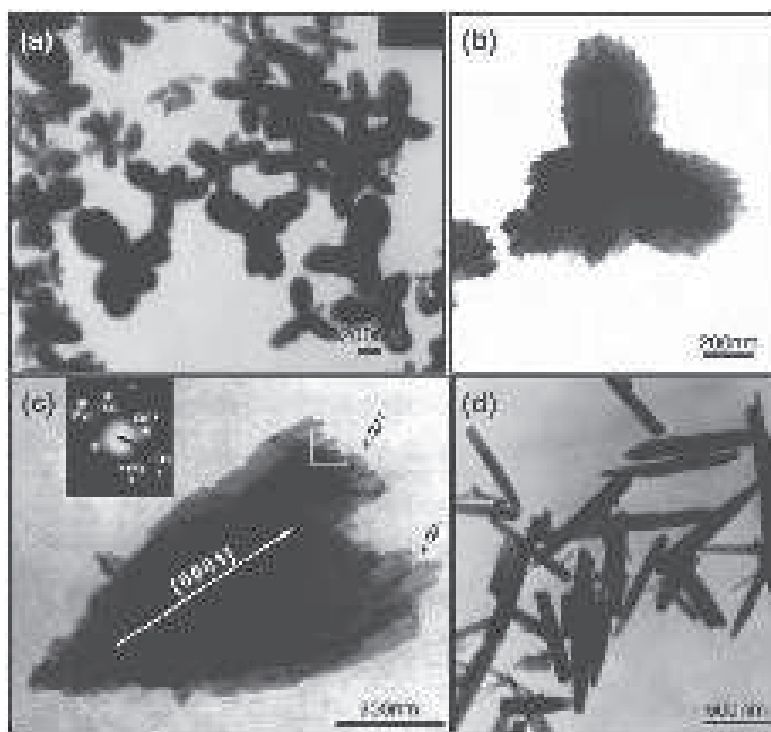


Figure 13. Micrographs showing multipetals of (a–c) ZnO nanomaterials prepared with β CD and (d) ZnO nanofibers prepared without β CD. Reproduced with permission from [77].

3. Cyclodextrins in membrane technology

Membrane technology is one of the methods that have been used in water treatment for decades. Its merits have made its use continuous throughout the decades; however, membranes have several demerits, which cannot be ignored. Membranes suffer from fouling, selectivity and low flux among other problems. This results in poor performance, which implies high operational cost for poor water output. Modifying membranes with materials such as nanomaterials and polymers via surface functionalization greatly improves the overall performance of membranes. Currently, polymeric membranes are the most used in water treatment because of their advantages, which include higher flexibility, easy pore formation mechanism, smaller footprint for installation and low cost compared to other membrane types [81–83]. When it comes to energy efficiency and cost-effectiveness, it is required that membranes should have high permeability, high rejection and good fouling properties [81].

The use of CDs and their derivatives has been found to enhance membrane performance in terms of improved porosity, flux, rejection and efficiency, which makes the use of CDs considerably effective. Porous CD-based membranes have interconnected pores with high permeability and find application in various filtration processes [84, 85]. Even though the use of CDs in membrane technology is not as advanced as the use of other polymers, several researchers have dedicated their time into studying and exploring new properties and advantages brought by CDs in various membrane types. The use of CDs in water treatment has been motivated by the ability of CDs to allow water to pass through their cavities and their surface

functionalities, which greatly improve the hydrophilicity and permeability of membranes [86]. Mixed matrix membranes (MMMs) and thin film composite (TFC) membranes are two types of membranes where CDs and their derivatives have been used as modifying agents to improve their total performance.

3.1. Mixed matrix membranes

Mixed matrix membranes (MMMs) are known for their high flux and low pressure drops. MMM high flux capacity and selectivity are often a result of functionalized modifying agents [87]. MMMs are used mostly for the removal of heavy metals, natural organic matter (NOM), EMPs and disinfection by products such as trihalomethanes, haloacetic acids, trihaloacetaldehydes, haloacetones and trihalonitromethanes in water [88]. Adams et al. prepared MMMs using polysulfone/ β CD-polyurethane (PSf/ β CD/PU) for the selective removal of Cd^{2+} ions and improved structural properties of PSf MMMs. Upon studying their characteristics, it was found that β CD-polyurethane enhanced the water sorption and hydrophilicity and achieved 70% removal of Cd^{2+} ions [18]. Adams et al. used the same material (PSf/ β CD/PU) in 2014 to study the effect of β CD/PU on the rejection of NOM and fouling resistance of PSf MMMs. It was concluded that β CD/PU improved the effective pore sizes and molecular-weight cut-off of PSf membranes due to their conical structure and larger pore sizes, which allows water molecules to pass easily [89]. Other workers used ceramic membranes modified with cross-linked silylated dendritic polymers and CDs for the removal of organic pollutants in water. The modified membranes removed pollutants such as monocyclic aromatic hydrocarbons (93%), pesticide (43%), polycyclic aromatic hydrocarbons (99%) and trihalogen methanes (81%). The high removal percentage was attributed to the dendritic polymers and CDs [90]. **Figure 14** shows

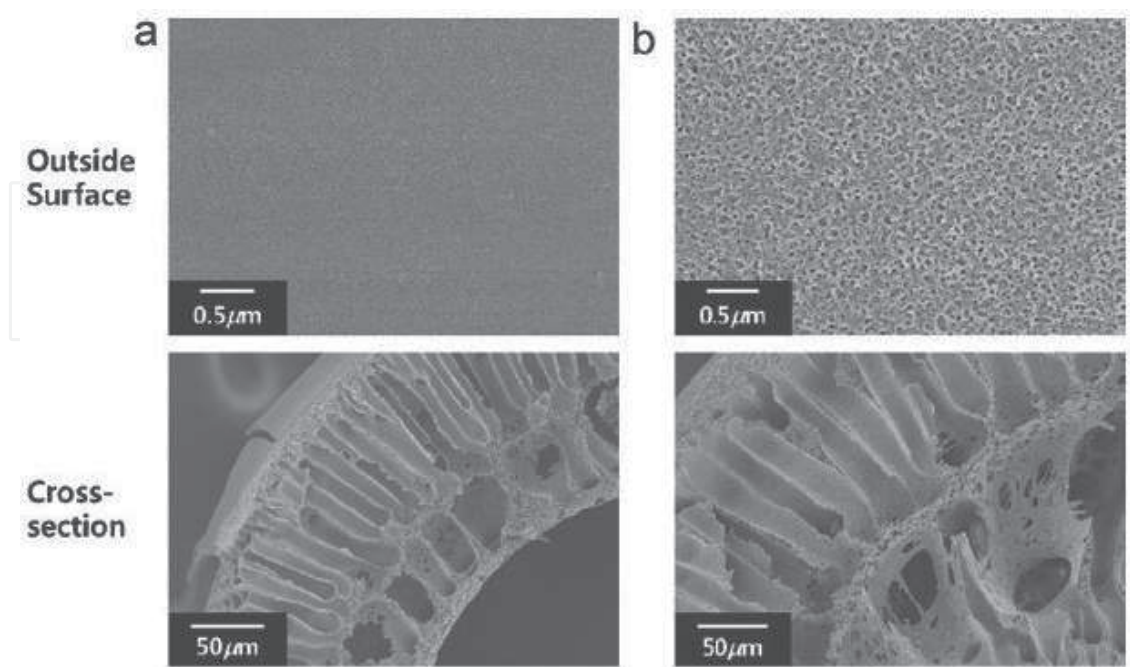


Figure 14. SEM images comparing morphologies for (a) PSf and (b) PSf/ β CD outside surface and cross-section. Reproduced with permission from [91].

comparison between PSf and PSf/ β CD membranes and it is shown that β CDs improved the surface and cross-sectional morphology in terms of pore size dimensions and size distribution.

3.2. Thin film composite membranes

Nanofiltration (NF) membranes are pressure-driven membranes and are mostly thin film composite (TFC) membranes [86]. TFC membranes include reverse osmosis (RO) and ultrafiltration (UF) membranes prepared by interfacial polymerization. The unique structure of TFC membranes that consists of a UF support, a nonwoven support and a polymer membrane brings advantages such as low operation pressure, high retention of multivalent ions or salts, low maintenance cost and high permeation flux [86, 92, 93]. This type of membranes is mostly used in water treatment for the production of drinking water from wastewater, seawater and brackish water [94]. Other areas of application include organic solvent nanofiltration and pharmaceuticals and biochemical industries [86, 93]. The layers of TFC membranes can be modified independently for maximum preferred properties such as water uptake, fouling resistance, chemical resistance, thermal stability, hydrophilicity and mechanical strength [92]. The excellent properties of TFC membranes are due to modifying agents such as CDs and their derivatives.

Wu et al. prepared NF TFC membranes using polyester/ β CD as a polymer material [81]. The addition of β CDs was found to improve the membrane performance as shown by double flux and high rejection of Na_2SO_4 compared to bare membranes. When sulfated- β CDs were used, the membrane had improved negative charge density and salt rejection. Both membranes were reported to have enhanced antifouling properties [86]. On the subject of TFC membranes, Mbuli et al. used amino-CDs and diethylamino-CDs to modify polyamide TFC membranes. The addition of modified CDs enhanced the membrane's permeability because of improved hydrophilicity and additional water channels. In a separate study, modified TFC membranes containing CDs also demonstrated high flux and good NaCl rejection [94]. Mao et al. prepared CD-modified PEI membranes for organic solvent nanofiltration. In the study, they

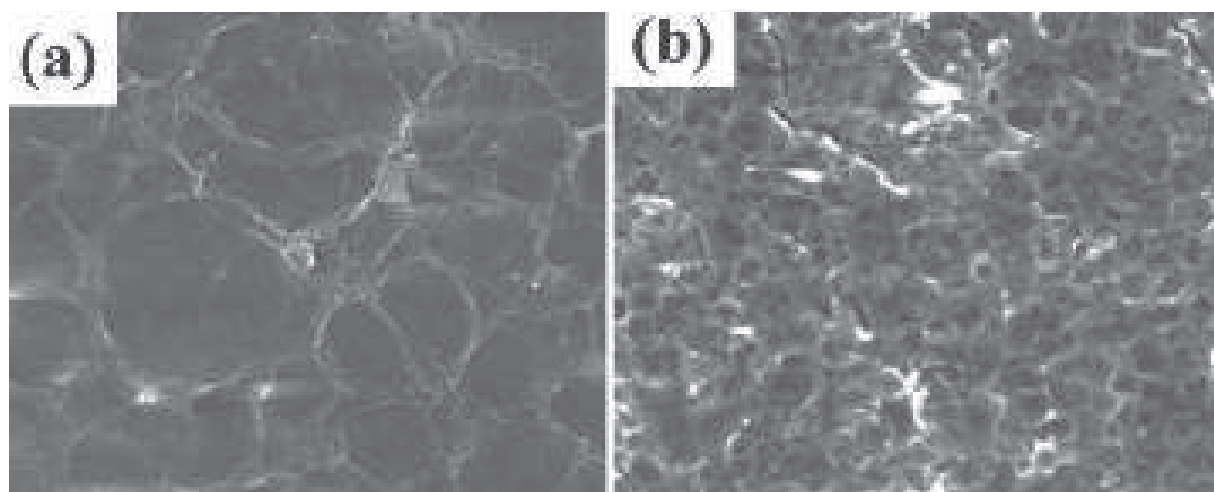


Figure 15. SEM images of (a) unmodified and (b) amine f-CD m-phenyldiamine TFC membranes. Reproduced with permission from [95].

Material	Type	Method	Application	Ref.
PSf-βCD-polyurethane	MMM	Phase inversion	Nanofiltration for removal of Cd ²⁺ ions	[18]
βCD-polyurethane	MMM	Phase inversion	Rejection of NOM (humic acid)	[89]
Azo dye-modified βCD-epichlorohydrin	MMM	Polymerization and phase inversion	Detection of chloroform, 1,3-dichloropropane, 1,2-dichloroethane, 1,2-dichloropropane, 1,1,2-trichloroethane and dichloromethane	[88]
Fe-Ni/f-CNT/βCD-polyurethane	MMM	Polymerization and precipitation	Degradation of trichloroethylene	[96]
PSf-βCD	MMM	Phase inversion	Removal of endocrine disruptive chemicals	[91]
CD-polymers	—	—	Adsorption and separation of pesticides	[97]
PES/m-phenyldiamine and PES/m-phenyldiamine/amine-f-CDs	TFC	Interfacial polymerization	Rejection of NaCl and Na ₂ SO ₄	[95]
PE/βCDs	TFC	Interfacial polymerization	Rejection of Na ₂ SO ₄ and antifouling properties	[86]
PA/amino-βCDs	TFC	Interfacial polymerization	Rejection of MgSO ₄ and fouling-resistant studies	[92]
PA/diethylamino-βCDs	TFC	Interfacial polymerization	Organic solvent nanofiltration	[93]
PEI/α, β and γCDs	TFC	Interfacial polymerization	Organic solvent nanofiltration	[93]
PA/amino-α and βCDs	TFC	Interfacial polymerization	Rejection of NaCl	[94]
PA/diethylamino-α and βCDs	TFC	Interfacial polymerization	Rejection of NaCl	[94]

Table 3. CDs and CD derivatives used as additives in traditional membranes.

prepared a membrane with dual pathway nanostructures from CDs (hydrophobic pathway) and the fractional free volume of PEI (hydrophilic pathway). Toluene permeation was improved from 0.13 to 2.25 L/mhbar when CD loadings were increased [93]. **Figure 15** shows m-phenylenediamine (a) and amine (b) f-CD-modified PES membranes. The presence of uniform pores is observed on membranes (b) due to the addition of amine f-CDs, while the addition of m-phenylenediamine produced membranes with layered structures on top (a). The incorporation of amine f-CDs improved the general performance of the membrane in terms of hydrophilicity, flux and salt rejection [95]. In **Table 3**, we show recent works on the use of CDs and their derivatives in the production of MMMs and TFC membranes.

4. Other applications of CD-based materials

The ability of CDs to form inclusion complexes with other materials and alter their properties has enabled electrospun CD-based materials and membranes to be used in many applications

such as drug delivery, filtration, templates, biomedical, catalysis, water treatment, reinforcement, electronics, pharmaceuticals and optical devices [39, 98, 99]. Celebioglu and coworkers formed inclusion complexation using the antibacterial agent, triclosan, with two types of CD derivatives (HP- β CDs and HP- γ CDs). The electrospun inclusion complexes were tested against Gram-negative (*Escherichia coli*) and Gram-positive (*Staphylococcus aureus*) bacteria. The antibacterial activity against the two bacteria strains was found to be higher for the inclusion complexes compared to the bare triclosan. The interactions of triclosan with the CD derivatives improved its antibacterial activity [100]. Li and coworkers used β CDs with maleic anhydride (MAH) and 3-(4-vinylbenzyl)-5,5-dimethylhydantoin (VBDMH) for antibacterial studies. The composite β CD-MAH-VBDMH was electrospun with cellulose acetate and the antibacterial activity was tested against *E. coli* and *S. aureus* bacteria. The nanofibers achieved 99.7 and 80.3% activity against *E. coli* and *S. aureus*, respectively, within 10–30 min contact time [20]. In another study, Dong and coworkers used ciprofloxacin hydrochloride (CipHCl) as the antibacterial agent with electrospun citric acid cross-linked cellulose and β CDs. The CipHCl loaded on the electrospun nanofibers demonstrated high antibacterial activity against *E. coli* and *S. aureus* [101].

In drug delivery systems, CDs and their derivatives have also been used for targeted delivery and control of release rate as well as solubility control. Bazhban and coworkers electrospun a drug delivery system from carboxymethyl- β CDs and chitosan blended with PVA in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide as the condensing agent and *N*-hydroxysuccinimide as a hydrolyzing agent. The electrospun nanofibrous mats were observed to have slower release rates of the entrapped salicylic acid compared to the nanofibrous mats without β CDs [64]. Canbolat and coworkers complexed naproxen (NAP) with β CDs and electrospun the inclusion complex with poly(ϵ -caprolactone) (PCL/NAP- β CDs). The electrospun PCL/NAP- β CDs had high release rates of NAP compared to the electrospun PCL/NAP [50]. Electrospun CD nanofibers have also been used in the syntheses of metal nanoparticles as reducing agents and size-controlling agents. Celebioglu and coworkers synthesized Ag nanoparticles in the presence of PVA/CD electrospun nanofibers. They obtained Ag nanoparticles of 2 nm in size without aggregation compared to the 8 nm aggregated nanoparticles obtained with the use of bare nanofibers [56]. Bai and coworkers used electrospun PVP/ β CDs as stabilizing and reducing agents for the synthesis of Au nanoparticles. The Au nanoparticles were found to be evenly distributed and well dispersed in the nanofibers and induced antibacterial behavior on the nanofibers [47].

By forming inclusion complexes with other materials, CDs can improve their stability and shelf life. Kayaci and coworkers enhanced the thermal stability of eugenol (EG) by means of inclusion complexation with β and γ CDs. The inclusion complex EG-CD was incorporated and electrospun together with PVA. The complexed EG demonstrated thermal evaporation at high temperature and slowed release at temperatures as high as 100°C compared to poor thermal stability of pure EG [66]. Uyar and coworkers prepared inclusion complexes between menthol with α , β and γ CDs and electrospun the complexes with polystyrene in order to enhance the thermal stability of menthol. The thermal stability of menthol was improved up to 350°C by the electrospun nanofibers [65].

This is an indication that electrospun CD nanofibrous mats have a wide range of applications. Whenever CDs are used, they enhance certain properties of the materials incorporated with to achieve excellent outcomes.

5. Mechanism for the interaction of CD nanofibers/membranes with various species

As discussed earlier, CDs and their derivatives have the ability to form inclusion complexes with a number of liquid, solid or gaseous compounds [12], which can alter the physicochemical properties of the guest molecule [102]. This happens by taking up a whole or part of a guest molecule into the hydrophobic cavity, which is lined by skeletal carbons as well as the ethereal oxygen of the glucose units. During the formation, no covalent bonds are made or broken, and as a result the guest molecule is not permanently hosted, it is rather in a dynamic equilibrium with the host [103–105]. **Figure 16** shows an example of an inclusion complex between a CD molecule and an organic compound. The hydrophobic cavity provides an environment for appropriate guests to settle in and form a complexation with the CD molecule [12]. In solid-state inclusion complexation, guest molecules can be enclosed within the cavity or can aggregate outside the CD, while solution state inclusion complexation is controlled by equilibrium between the complexed and noncomplexed molecules [102, 106]. For successful inclusion complexation to occur the guest or part of the guest must have the size, polarity and shape that are compatible with those of the host [107]. Physicochemical properties of

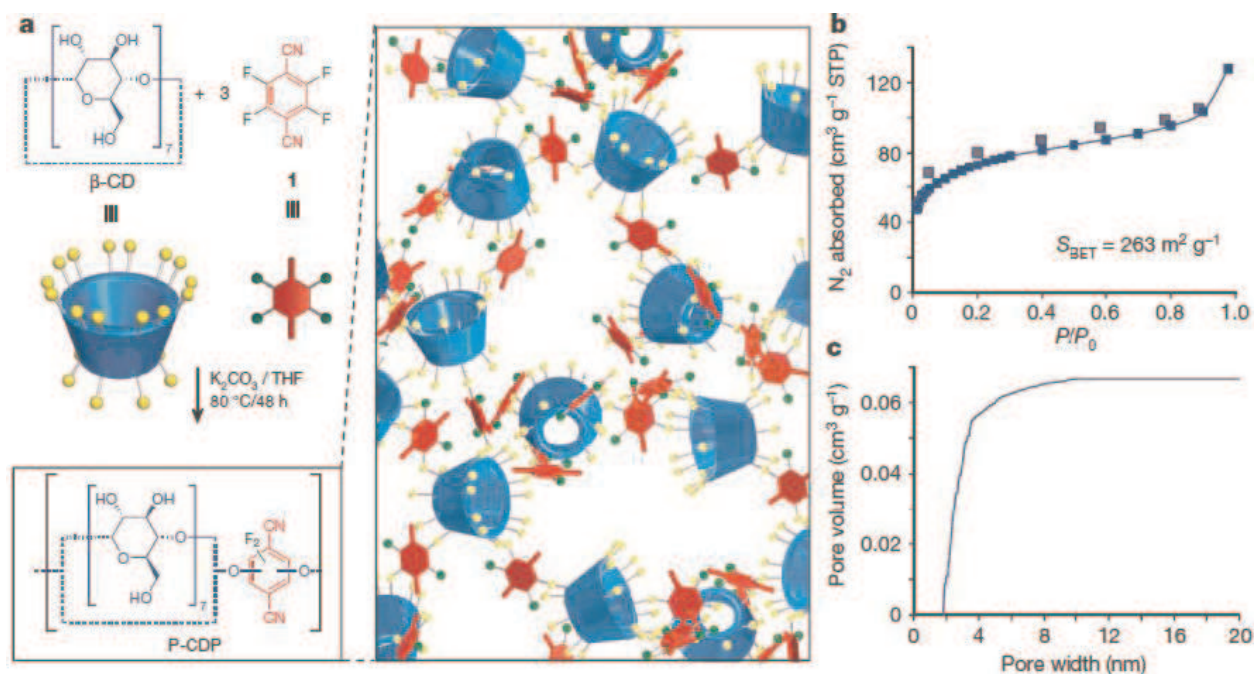


Figure 16. Illustration of (a) interaction of βCD with an organic molecule forming a polymeric network, (b) N₂ adsorption and desorption and (c) pore volume measurements of the polymeric structure. Reproduced with permission from [109].

guests that can be altered during inclusion complexation include taste modification, solubility enhancement, physical isolation and stabilization of labile guests [108]. As shown by **Figure 16**, CDs and their derivatives can interact with other molecules to form supramolecular polymeric structures [109]. The high surface area and pore volume and permanent porosity of the porous CD polymer enable the rapid removal of the organic contaminants [109].

Marques et al. used CDs for the encapsulation of essential oils such as chamomile oil via inclusion complexation. Inclusion complexation of essential oils is used for various reasons such as avoiding degradation induced by oxygen, light or heat, improving water solubility and stabilizing fragrances [110]. β CDs were also used by others to enhance the solubility of Gliclazide by employing the coprecipitation and kneading methods. It was found that the complex prepared by kneading method was more suitable for the improvement of Gliclazide solubility compared to the one prepared by coprecipitation [111].

By inclusion complexation, the CD moiety does not only bind the guest molecules but also brings them close to the functional groups for other reactions such as photocatalytic degradation to take place [112]. CDs can also alter the physicochemical properties of the guest molecules by making it easy to modify during that period. For example, it can promote fast dissolution rates, efficient absorption and short drug release times. As a result, CDs find application in cosmetics, food, drug delivery, bioconversion and environmental protection [103, 105]. It should be noted that complexation between the host and a guest depends mostly on several properties of the host and guest, dosage, thermodynamics and equilibrium kinetics.

The index of the change in physicochemical properties of guest can be shown by the stability, equilibrium constant (K_c) and dissociation constant (K_d) measurements. The formation of inclusion complexation toward equilibrium is assisted by four energetically favorable interactions, which are:

- i. The displacement of water molecules from the hydrophobic cavity by nonpolar molecules.
- ii. The increasing number of hydrogen bonds formed when the displaced water is driven to the outer pool.
- iii. Reduced repulsive interactions between the nonpolar guest and the aqueous environment.
- iv. Increasing hydrophobic interactions as the guest inserts itself into the cavity [12].

Clearly, the common interaction of CDs with other species in aqueous solutions is inclusion complexation. Kayaci and coworkers reported that the filtration efficiency of PET was improved after surface modification with α , β and γ CD. The filtration process was tested against phenanthrene compounds and the improvement was credited to inclusion complexation between the CDs and phenanthrene [7]. Uyar and coworkers reported the use of PMMA nanofibers modified with β CD for molecular entrapment of organic vapors such as styrene, aniline and toluene. The reported interaction between the vapors and nanofibers was inclusion complexation (CD) and adsorption (PMMA and CDs). The interactions between the two were analyzed by direct pyrolysis mass spectrometry and thermogravimetric analysis [51].

Chen and coworkers prepared a molecular filtration membrane using carbonaceous nanofiber membranes (CNFs) modified with β CDs for the filtration of phenolphthalein in aqueous solutions. Again, the removal of this compound was credited to complexation with CDs and absorption by both CDs and CNFs [63]. Workers reported the reduction of Ag and Fe supported on β CD/cellulose acetate nanofiber membranes for antibacterial studies. The CD molecules facilitated the charge transfer that occurred between ionized water molecules and Ag^+ and Fe^{3+} since they were able to alter physicochemical properties of guest molecules (and in this case metal nanoparticles) [17].

Several publications reported the use of CDs in various applications such as drug delivery, catalysis, water and air treatment, sensors and energy storage devices. The outstanding performance of all the materials is credited to inclusion complexation and absorption ability that are caused by hydrophobic and intermolecular interactions between the compounds of interest and CDs [16, 64, 113, 114].

6. Characterization tools for CD materials

There are several methods that can be used to study and understand the properties and characteristics of CDs, CD-derivatives and CD-guest inclusion complexes. To study, understand and confirm changes on CD physicochemical properties during applications, analysis has to be conducted using a series of conventional techniques that can complement each other and give conclusive data. Some of the techniques are discussed in the subsections below.

6.1. X-ray diffraction

X-ray diffraction (XRD) is very useful for the analysis of CD materials in powder or microcrystalline states. This is simply because the XRD pattern of the parent CD will be different from that of the derivative or the inclusion complex, which will confirm successful modification, functionalization and/or inclusion complexation [110, 111]. This technique can be used on ground and homogenized samples even on unknown samples. The intensity of peaks helps understand the interactions between CDs and other materials as well as their degree of crystallinity [115].

6.2. Nuclear magnetic resonance

Nuclear magnetic resonance (NMR) is mostly used to study inclusion complexation in solution and has been very useful in understanding the bonding configuration of functionalities present. This is mostly because when a guest is hosted the interior hydrogens are shielded by the guest resulting in a shift on the NMR spectroscopy [110]. NMR can also be used to determine the atoms that stabilize host-guest complexes using ^{13}C -NMR by monitoring the shifts of the carbon atoms involved [110, 115]. Furthermore, NMR can also provide information on the orientation of the guest within the host's cavity [115, 116].

6.3. Infrared spectroscopy

Infrared spectroscopic techniques such as the Fourier transform infrared (FTIR) spectroscopy can be used to reveal CD functionalization and inclusion complexation. This can be validated by the appearance of new peaks, shift in peak position or change in peak intensity as a result of changes on pure CD molecules. Noticeable changes may include disappearance of the —OH peak for functionalization with the appearance of new peaks depending on the type of functional groups introduced. For inclusion complexation, —CO stretching peaks may be observed [110]. Vibrational modes of the host and guest can be studied using this technique to understand the process of complexation and/or functionalization. Vibrational modes can be restricted to a certain level during complexation and this can result in weak interatomic bonds due to the altered environment around the bonds [116, 117].

6.4. Ultraviolet/Visible spectroscopy

The absorption properties of the host and guest molecules (such as dyes) can be easily altered by functionalization or inclusion complexation. When that happens, ultraviolet-visible spectroscopy confirms the successful complexation or functionalization by monitoring the band broadening or narrowing and/or bathochromic shift [110]. In fact, inclusion complexation can result in hypsochromic or bathochromic shift and/or increase or decrease in the intensity of the absorption maxima. However, this technique does not provide conclusive results on complexation or functionalization [116, 118].

6.5. Fluorescence spectroscopy

The environment of molecules can greatly influence their fluorescence properties; hence, fluorescence spectroscopy can be used to determine the geometry of complexation. Fluorescence quantum yield is high in complex formation and the maxima emission is often shifted to shorter wavelengths [110]. The enhancement of fluorescence in complexation is a result of shielding caused by quenching and nonradioactive decay processes [116]. This technique can only be used for fluorescent molecules.

6.6. Differential scanning calorimetry

Differential scanning calorimetry (DSC) is an analytical technique based on thermal analysis of compounds. For physical and energetic properties, DSC is one of the most used techniques for CD complexation especially in CD-drug complexes. Endothermal dehydration peaks and decomposition peak are the main characteristics of CDs and are found at $90\text{--}130^\circ\text{C}$ and 300°C , respectively. The appearance of a sharp enhanced endothermal peak indicates the formation of a host-guest complex, which is a sum of the individual compound peaks. Since physicochemical properties of guests can be changed during complexation, DSC can show the loss of guest crystallinity by broadening, size reduction and lower temperature shift of guest-melting peaks [116, 119]. However, guest-melting peaks may also indicate the presence of free guest molecules meaning that equilibrium has been reached [120]. In this case, chromatographic techniques can be used to separate the complex and free molecules.

6.7. Chromatography

Chromatographic analysis such as thin layer chromatography (TLC) can be very useful for the verification of complexation and modification by monitoring the alterations of the retardation factor R_f values. The complex of modified CDs is found between the R_f values of the CDs and that of the functional group or guest [110, 121]. Another way to study CDs and their complexes using chromatography is by monitoring their volatility using head-space chromatography. This chromatographic technique is specifically for volatile compounds. The increase or decrease in volatility can be observed as influenced by the host-guest interaction and the stability of the complex can be determined [110, 122].

6.8. Microscopic techniques

Microscopic techniques such as SEM and TEM are used as complementary techniques to analyze the surface morphology, topography and composition of various samples including nanofibers and membranes containing CD species. These two techniques give critical details on the size, size distribution and alignment of fibers as well as the nature of the nanofiber or membrane surfaces. These microscopic techniques are mostly used in the analytic investigation of nanofibers and membranes because of their capability of imaging at high resolutions [11, 43, 49, 69, 73, 77].

6.9. Other characterization techniques

Other popular techniques often used to study CDs, their derivatives and nanocomposites are thermogravimetric analysis to probe their thermal stability, circular dichroism spectroscopy to study inclusion complexation of ideally sized molecules in the CD cavity, contact angle analysis to understand the hydrophilicity of surfaces, nanosizer instruments for surface charge and Brunauer-Emmett-Teller (BET) to measure the surface area and pore volume.

7. Toxicology and safety of CDs and their derivatives

Even though CDs have several advantages for applications in areas such as water treatment, tissue engineering and drug delivery, their toxicity, biological fates and safety issues need to be evaluated since they eventually find their way into animal and human bodies. The three most common natural CDs and their hydrophilic derivatives are known to only permeate lipophilic biological membranes, which include the gastrointestinal mucosa, skin and cornea of the eye with certain difficulty. CDs have been reported to be nontoxic to a certain level due to low absorption from the gastrointestinal track [12, 123, 124]. α CDs were found to bind with some lipids resulting in eye irritation in rats when they were orally administered, whereby 60% of the dose was excreted as CO_2 , 26–33% as metabolite incorporation and 7–14% as metabolites in urine and feces [12, 125]. Oral administration in rats showed that β CDs have less irritation compared to α CDs; however, small amounts were absorbed in the upper intestinal track [12, 126]. Even though they are nontoxic when administered orally, β CDs cannot be administered parenterally due to their low solubility in aqueous solutions and their nephrotoxicity [127].

Oral administration of γ CDs has insignificant irritation followed by rapid and complete degradation to glucose by intestinal enzymes. They are therefore deemed the least toxic [12, 128]. α and β CDs are also known for their renal toxicity [127]. β CD is not used in parenteral formulations and the use of α CD is seriously limited due to toxicological consideration [123]. Parent CDs (α and β) and lipophilic CD derivatives such as m- β CD are also not suitable for parenteral formulation due to their rapid absorption by the gastrointestinal track; however, they are suitable for oral formulations [123, 127].

The newly discovered CD derivatives with better safety profiles have sparked a renewed interest in the use of CDs, especially for those that will find way into human and animal bodies. For example, HP- β CDs and sulfobutylether- β CDs are used in parental formulations in very high concentrations [123, 129]. The concentration, type of administration and time of exposure play a critical role in determining the level of toxicity and safety of CDs and their derivatives. It is therefore generally thought that CDs and their derivatives can be safely used in membrane technology and other applications without toxicological problems in case they leach out and be ingested by humans or animals, especially in areas such as wound dressing, water treatment and air purification.

8. Challenges and perspectives

One of the major challenges in the production of CD nanofibers is the inability to electrospin CDs directly, i.e., without the need to blend them with other copolymers or modifying their structure. The poor solubility of CDs in water and organic solvents makes it impossible to electrospin CDs directly. Hence, the most feasible way is to blend the CDs with other flexible polymers. Indeed, many studies have reported the fabrication of CD-based nanofibers using copolymers. In membrane technology, the main challenge is their high water solubility, which results in the loss of structure and functionality of membranes once the CDs are dissolved and washed away.

The application of these materials varies significantly. Workers are currently exploring the commercial viability of CD-based fibers especially in areas of water treatment. Their use in various applications is possible due to their ability to form inclusion complexes with various compounds. The chemistry responsible for this complexation is now well understood. The performance of CD-based materials can thus be ascertained or monitored using simple phase-solubility diagram.

Further, the high surface area-to-volume ratio of nanofibers and modification possibilities of CD molecules have motivated the use of CD nanofibers in areas such as tissue engineering and water treatment. The nanofiber morphology is preferred over other morphologies of the CD polymers, which tend to possess lower surface areas. The electrospinning technique can now produce large quantities of nanofiber membranes and makes it viable to use the materials in large-scale quantities. However, the cost is yet to be ascertained.

9. Conclusion

In general, CDs are less toxic and environment-friendly materials due to their biodegradable nature. CDs and their derivatives have unique properties such as high porosities,

small diameters and high surface area-to-volume ratio rendering them practically usable in a wide range of applications including water treatment. Indeed, electrospinning these glycosidic sugars into nanofibrous mats improves their surface area-to-volume ratio further and enhances their adsorption and inclusion complexing properties. Undesirable species of specific sizes can be encapsulated *via* inclusion complexation and filtered by CD-based nanofibers and membranes. Electrospun CD nanofiber mats and membranes find further applications in various areas such as drug delivery, filtration, catalysis, water treatment, reinforcement, electronics, pharmaceuticals and optical devices. Considering that they are natural, nontoxic, cost-effective and readily available, their properties can be explored for further applications. Scaling-up and subsequent commercialization of these superior nanofibers and membranes can be explored once their cost has been determined.

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